PERSPECTIVES

A new answer to an old question: does ageing modify baroreflex control of vascular sympathetic outflow in humans?

Kevin D. Monahan
Penn State Heart and Vascular Institute, Pennsylvania State University College of Medicine, The Milton S. Hershey Medical Center, 500 University Drive, Hershey, PA 17033-2390, USA

Email: kmonahan@psu.edu

The baroreflexes are the primary neural mechanism by which arterial blood pressure (BP) is regulated on a beat-by-beat basis. Over 100 years of research has provided great insight into the structure and function of the baroreflexes in both health and disease (Eckberg & Sleight, 1992). In humans baroreflex function is commonly quantified by assessing changes in R–R interval or vascular sympathetic outflow during dynamic increases and/or decreases in BP. With advancing age, it is well accepted that baroreflex modulation of R–R interval is depressed (Monahan, 2007). In contrast, although less thoroughly studied, baroreflex control of vascular sympathetic outflow is generally believed to be unchanged with advancing age (Monahan, 2007).

In this issue of *The Journal of Physiology,* Studinger *et al.* (2009) provide a new answer to an old question: does ageing alter baroreflex control of vascular sympathetic outflow in humans? Based upon their new data (Studinger *et al.* 2009), the simple answer to this question appears to be 'yes'. However, whether ageing impairs or augments baroreflex control of vascular sympathetic outflow critically depends on whether the baroreflexes are responding to increases or decreases in BP. Specifically, the authors observed impaired sympathetic activation during BP falls and augmented sympathetic inhibition during BP increases. The ability to identify these divergent effects of ageing on baroreflex control of vascular sympathetic outflow was dependent on the authors' careful consideration and analysis of the data. The viewpoint that hysteresis is not present in the sympathetic arm of the baroreflex (Rudas *et al.* 1999) was challenged (Studinger *et al.* 2009). This analysis revealed that hysteresis was indeed present in the sympathetic arm of the baroreflex in both young and older adults (Studinger *et al.* 2009). The presence of hysteresis necessitated that data obtained during periods in which BP was increasing and decreasing be *separately* considered and analysed and not combined ('pooled') into a single analysis as previously recommended (Rudas *et al.* 1999).

To provide insight into the site at which baroreflex changes occurred with ageing, carotid arterial imaging was performed during assessments of baroreflex function (Hunt *et al.* 2001). This allows the 'integrated' baroreflex response (vascular sympathetic outflow–BP relation) to be broken into its mechanical (carotid diameter–BP relation) and neural components (vascular sympathetic outflow–carotid diameter relation). These analyses revealed a smaller mechanical component of the baroreflex with ageing during both increases and decreases in BP (Studinger *et al.* 2009), consistent with the detrimental effect ageing exerts on large artery stiffness. Importantly, during increases in BP the neural component of the baroreflex was augmented to such a degree by age that it completely overcame the negative effects of ageing on the mechanical component of the baroreflex, resulting in increased integrated gain. In contrast, during decreases in BP, an enhanced neural component of the baroreflex was insufficient to overcome the effect of age on the mechanical component of the baroreflex, resulting in decreased integrated gain. Collectively, these data illustrate: (1) the importance that age-associated changes in large artery function exert on the sympathetic arm of the baroreflex, and (2) that the sympathetic arm of the baroreflex possesses an impressive level of neural plasticity with advancing age in humans. Of equal importance, similar age-associated changes in the sympathetic arm of the baroreflex occur in men and women and changes in baroreflex control of vascular sympathetic outflow were not influenced by habitual endurance exercise in older men (Studinger *et al.* 2009).

The finding that baroreflex control of vascular sympathetic outflow is impaired with age in response to decreases, but not increases, in BP is interesting and may be of clinical importance. For instance, this finding may provide an explanation as to why hypotensive responses to certain vasodilator medications increase with age while the local vascular response remains unchanged (e.g. nitroprusside).

By documenting hysteresis in the sympathetic arm of the baroreflex Studinger provides important new insight into the effect ageing, sex, and endurance-training status exert on baroreflex control of vascular sympathetic outflow in humans (Studinger *et al.* 2009). These findings should serve as a careful reminder to all investigators to adopt rigorous analysis techniques in future studies. Moreover, they may make us reflect on the validity of previous findings in which hysteresis in the sympathetic arm of the baroreflex may not have been fully considered and appreciated.

References

Eckberg DL & Sleight P (1992). *Human Baroreflexes in Health and Disease*. Clarendon Press, Oxford, UK.

Hunt BE, Fahy L, Farquhar WB & Taylor JA (2001). *Hypertension* **37**, 1362–1368.

Monahan KD (2007). *Am J Physiol Regul Integr Comp Physiol* **293**, R3–R12.

Rudas L, Crossman AA, Morillo CA, Halliwill JR, Tahvanainen KU, Kuusela TA & Eckberg DL (1999). *Am J Physiol Heart Circ Physiol* **276**, H1691–1698.

Studinger P, Goldstein R & Taylor JA (2009). *J Physiol* **587**, 2049–2057.

DOI: 10.1113/jphysiol.2009.172056